Disease Name	**Short-Chain Acyl-CoA Dehydrogenase Deficiency**
Acronym	SCADD or SCAD
Disease Classification	Fatty Acid Oxidation Disorder
Variants	Yes
Variant name	Late-onset with chronic myopathy
Symptom onset	Neonatal - but very variable; may be asymptomatic.
Symptoms	Neonatal - failure to thrive, hypotonia, metabolic acidosis, seizures and developmental delay.
Natural history	Developmental delay, hypotonia and muscle weakness have been observed, but the vast **without treatment** majority of patients detected via MS/MS newborn screening have been entirely asymptomatic.
Natural history with treatment	The efficacy of treatment is unknown.
Treatment	Carnitine supplementation, restriction of dietary fat. A few patients have shown improvements on riboflavin supplements.
Other	Acute fatty liver of pregnancy and HELLP syndrome have been reported as maternal complications in pregnancy, but may be coincidental.
Emergency Medical treatment	See sheet from **American College of Medical Genetics** (attached) or for more information, go to website: **http://www.acmg.net/StaticContent/ACT/C4.pdf**
Physical phenotype	None reported
Inheritance	Autosomal recessive
General population incidence	1:40,000 – 1:100,000
Ethnic differences	None
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondrial matrix in liver, muscle, fibroblasts
Enzyme Function	
Missing Enzyme	Short-chain acyl-CoA dehydrogenase
Metabolite changes	Ethymalonic acid in urine, methylsuccinate and butyrylglycines in urine.
Gene	ACADS
Gene location	12g22-qter
DNA testing available	Yes - but interpretation of results is difficult.
DNA testing detail	Limited mutational hotspots and common susceptibility alleles
Prenatal testing	Enzymatic
MS/MS Profile	Elevated C4 Cbutyrylcarnitine
OMIM Link	http://www.ncbi.nlm.nih.gov/omim/606885
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Save Babies through Screening Foundation http://savebabies.org

Newborn Screening ACT Sheet
[Elevated C4 Acylcarnitine]
Short-Chain Acyl-CoA Dehydrogenase (SCAD) Deficiency

Differential Diagnosis: Short-chain acyl CoA dehydrogenase (SCAD) deficiency; Isobutyryl-CoA dehydrogenase (IBDH) deficiency (also referred to as isobutyrylglycinuria (IBG)); Ethylmalonic encephalopathy (EE).

Condition Description: SCAD deficiency is a fatty acid oxidation (FAO) disorder. FAO occurs during prolonged fasting and/or periods of increased energy demands (fever, stress) when energy production relies increasingly on fat metabolism. IBG results from IBDH deficiency. IBDH is an enzyme involved in the degradation of the branched chain amino acid valine. EE is a related disorder that seems to be due to a defective mitochondrial matrix protein, the precise function of which is yet unknown. In all three conditions, potentially toxic metabolites accumulate.

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy).
- Consultation with pediatric metabolic specialist.
- Evaluate infant (hypoglycemia, lethargy, metabolic acidosis).
- Emergency treatment if symptomatic.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Educate family about need for infant to avoid fasting and explain signs, symptoms and need for urgent treatment if infant becomes ill.
- Report finding to newborn screening program.

Diagnostic Evaluation: In SCAD deficiency urine organic acids show increased ethylmalonic acid. In IBG, plasma and urine acylcarnitines will show increased isobutyrylcarnitine (C4-acylcarnitine) and urine organic acids/acylglycine may show isobutyrylglycine. In EE, plasma acylcarnitine analysis will typically show C4- and C5-acylcarnitine and urine organic acids/acylglycine analysis will show increased EE and isovalerylglycine. Molecular genetic analysis to confirm the suspected diagnosis is possible for these conditions.

Clinical Considerations: SCAD deficiency can have a variable presentation. Most affected neonates are asymptomatic. An affected neonate however, can be extremely ill with vomiting, lethargy, seizures, and hypoketotic hypoglycemia. Treatment consists primarily of avoidance of fasting and vitamin/cofactor supplementation. Isobutyryl-CoA dehydrogenase deficiency may be benign (anemia and cardiomyopathy has been reported in one case). EE encephalopathy presents in infancy with developmental delay, diarrhea, and petechiae.

Additional Information:

New England Consortium of Metabolic Programs
OMIM EE

Referral (local, state, regional and national):

Testing
Clinical Services